

REMARKS

Claims 1-20 were acted on by the Examiner in the Action, dated 26 November 2010. Claims 1, 12-15, and 18-20 are amended. No claims are added. Claims 2-11, 16, and 17 are cancelled. Accordingly, claims 1, 12-15, and 18-20 are presented for examination.

Support for the amendment to claim 1 is found, for example, in original claims 11, 16, and 17. Claims 12-15, and 18-20 are amended for clarity, to update dependencies, and to correct antecedent basis issues.

No new matter is added.

Election/Restrictions

Applicants respectfully submit that there is a typographical error on Page 2, line 7, of the Action. The reply should read “Claims 21-62 are withdrawn...” instead of “Claims 6-21 are withdrawn...”.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants amend and traverse as follows.

Claim 1 is amended to recite the use of MutL, MutS, and antimutator alleles of *din B10* and *dnaE911* in order to reduce the spontaneous mutation frequencies in *E. coli*. Claims 2-11, 16, and 17 are cancelled without prejudice. Applicants respectfully submit that this amendment identifies structural properties such that what is being claimed can be identified.

Accordingly, applicants respectfully request that the rejection of claims 1-20 under 35 U.S.C. 112, second paragraph, be withdrawn.

Rejections Under 35 U.S.C. § 112- Written Description

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicants amend and traverse as follows.

On page 5 of the Action, the Examiner states that:

The mutations which possess written description are in *E. coli* only and include at least two mutations selected from:

A mutation leading to an up-regulation of the expression of the MutL protein;

A mutation leading to an up-regulation of the expression of the MutS protein:

Introduction of antimutator allele *dinB10* (to the cell; and,

And introduction of antimutator allele *dnsE911* (a gene encoding a subunit of DNA polymerase III).

Claim 1 is amended to recite the use of MutL, MutS, and antimutator alleles of *din B10* and *dnaE911* in order to reduce the spontaneous mutation frequencies in *E. coli*. Claims 2-11, 16, and 17 are cancelled without prejudice. In order to advance prosecution, Applicants respectfully submit that this amendment is in accordance with the Examiner's statement on Page 5 of the Action.

Accordingly, applicants respectfully request that the rejection of claims 1-20 under 35 U.S.C. 112, first paragraph (written description), be withdrawn.

Rejections Under 35 U.S.C. § 112- Enablement

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Applicants amend and traverse as follows.

On page 9 of the Action, the Examiner states that:

The mutations which possess written description are in *E. coli* only and include at least two mutations selected from:

A mutation leading to an up-regulation of the expression of the MutL protein;

A mutation leading to an up-regulation of the expression of the MutS protein:

Introduction of antimutator allele *dinB10* (to the cell; and,

And introduction of antimutator allele *dnsE911* (a gene encoding a subunit of DNA polymerase III).

Claim 1 is amended to recite the use of MutL, MutS, and antimutator alleles of *din B10* and *dnaE911* in order to reduce the spontaneous mutation frequencies in *E. coli*. Claims 2-11, 16, and 17 are cancelled without prejudice. In order to advance prosecution, Applicants respectfully submit that this amendment is in accordance with the Examiner's statement on Page 5 of the Action.

Accordingly, applicants respectfully request that the rejection of claims 1-20 under 35 U.S.C. 112, first paragraph (enablement), be withdrawn.

Sequence Listing

The specification was amended to comply with the Sequence Listing rules in a separate Reply, filed on 17 December 2010.

Rejections Under 35 U.S.C. § 103

Claims 1-15 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foster et al (PNSA. 92: 7951-7955. 1995) and Jingyong et al (J. Bacteriol. 2000. 182(17): 5025-5028).

Applicants amend and traverse as follows.

On page 9 of the Action, the Examiner states that:

The mutations which possess written description are in *E. coli* only and include at least two mutations selected from:

A mutation leading to an up-regulation of the expression of the MutL protein;

A mutation leading to an up-regulation of the expression of the MutS protein;

Introduction of antimutator allele *dinB10* (to the cell; and,

And introduction of antimutator allele *dnsE911* (a gene encoding a subunit of DNA polymerase III).

Claim 1 is amended to recite the use of MutL, MutS, and antimutator alleles of *dinB10* and *dnaE911* in order to reduce the spontaneous mutation frequencies in *E. coli*. Claims 2-11, 16, and 17 are cancelled without prejudice.

Applicants submit that the presently claimed invention is non-obvious due to the secondary consideration of unexpected results.

Table 2 on page 51 of the application contains data which demonstrates the reduced mutatability of strains that overexpress mutL, or have mutations in *dinB10* or *dnaE*.

E. coli MG1655 *dinB10* containing plasmid pmutL (DSM 17016) has a mutation rate of 0.068, which is 4.55 fold below the mutation rate of wild type MG1655 strain.

E. coli MG1655 *dnaE* : cm containing plasmid pmutL (DSM 17018) has a mutation rate of 0.024, which is 12.91 fold below the mutation rate of wild type MG1655 strain.

E. coli MG1655dinB10 dnaE zae :: cm (DSM 17015) has a mutation rate of 0.032, which is 9.68 fold below the mutation rate of wild type MG1655 strain.

E. coli MG1655dinB10 dnaE zae :: cm containing plasmid pmutL (DSM 17020) has a mutation rate of 0.024, which is 12.91 fold below the mutation rate of wild type MG1655 strain.

These results demonstrate synergy in prevention of mutation when at least two of 1. overexpression of mutL, 2. dinB10 mutation, or 3. dnaE mutation are combined. The cited references, alone or in combination do not suggest a rate close to any of the mutation rates of the above strains. Accordingly, the claimed strains are inventive and non-obvious over the cited references.

Accordingly, applicants respectfully request that the rejection of claims 1-20 under 35 U.S.C. 103, as being as being unpatentable over Foster et al. and Jingyong et al., be withdrawn.

The applicants reserve the right to prosecute, in one or more patent applications, the canceled claims, the claims as originally filed, and any other claim that is supported by the instant specification. In view of the foregoing amendments and remarks, the applicants respectfully submit that the subject application is in condition for allowance. If the Examiner has any remaining objections or concerns, the applicants invite her to contact the applicants' undersigned attorney at the below telephone number to resolve such issues and advance this application to issue.

Respectfully submitted,

/Jonathan M. Dermott/

Jonathan M. Dermott
Attorney for Applicants
Registration No. 48,608

GLAXOSMITHKLINE
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939
Phone (610) 270-6887
Facsimile (610) 270-5090